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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/903,393	07/10/2001	Keith D. Allen	R-387	9468

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DELTAGEN, INC.
1003 Hamilton Avenue
Menlo Park, CA 94025

EXAMINER	
SHUKLA, RAM R	
ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 12/05/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/903,393	ALLEN, KEITH D.	
	Examiner	Art Unit	
	Ram R. Shukla	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-29* is/are pending in the application.

4a) Of the above claim(s) *1-7,13,14,16 and 25-29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-12,15 and 17-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10 July 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicant's election without traverse of the invention of group III, claims 8-12, 15 and 17-24 in Paper filed 9-22-2003 is acknowledged.

2. Claims 1-7, 13, 14, 16, and 25-29 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper filed 8-22-2003.

3. Claims 8-12, 15, and 17-24 drawn to a transgenic non-human animal comprising a disruption in a limulus clotting factor protease-like gene, a method of producing a transgenic mouse comprising a disruption in a limulus clotting factor protease-like gene, cells of the transgenic mouse/non-human animal and a method of using the transgenic mouse/non-human animal and its cells for identifying agents that modulates the expression of a limulus clotting factor protease-like gene are under prosecution.

Specification

4. The attempt to incorporate subject matter into this application by reference to US non-provisional and provisional applications on pages 10 and 11 is improper because these applications are not related to the instant application and these applications are not published. Therefore, an artisan would not have access to these applications.

For any response to this office action to be complete, applicants are required to address this issue.

5. The specification is also objected to because the description of figures, figures and sequence listings do not match. It is noted that the specification states that SEQ ID NO 1 is the sequence of figure 1 and encodes the amino acid sequence of SEQ ID NO 2. However, the sequence of SEQ ID NO 1 and that disclosed in figure 1 are not the same and no amino acid sequence is listed in the sequence listing.

For the response to this office action to be complete, applicants are required to address this issue.

6. **Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.**

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Specifically the application fails to comply with CFR 1.821(d), which states:

(d) Where the description or claims of a patent application discuss a sequence that is set forth in the "Sequence Listing " in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the sequence identifier, preceded by "SEQ ID NO: " in the text of the description or claims, even if the sequence is also embedded in the text of the description or claims of the patent application.

For example, the specification discloses nucleotide sequences in figure 1. However, these sequences are not identified by sequence identifiers in the brief description of the figures and have not been listed in the sequence listing.

For compliance with sequence rules, it is necessary to include the sequence in the "Sequence Listing" and identify them with SEQ ID NO. In general, any sequence that is disclosed and/or claimed as a sequence, i.e., as a string of particular bases or amino acids, and that otherwise meets the criteria of 37 CFR 1.821(a), must be set forth in the "Sequence Listing." (see MPEP 2422.03).
For the response to this office action to be complete, Applicants are required to comply with the Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Claim Rejections - 35 USC § 101

7. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

8. Claims 8-12, 15, and 17-24 are rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility.

The claimed invention is drawn to a transgenic non-human animal comprising a disruption in a limulus clotting factor protease-like gene, a method of producing a transgenic mouse comprising a disruption in a limulus clotting factor protease-like gene, cells of the transgenic mouse/non-human animal and a method of using the transgenic mouse/non-human animal and its cells for identifying agents that modulates the expression of a limulus clotting factor protease-like gene.

When determining whether an applicant has described the utility of invention, one has to determine whether the applicant has described a well-established utility. If not, has the application made any assertion of specific, substantial and credible utility. A credible utility is assessed from the standpoint of whether a person of ordinary skill in the art would accept that the recited or disclosed invention is currently available for use. In contrast to general utility, a specific utility will be specific to the claimed subject matter. A substantial utility defines a real world utility of the invention and utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context use are not substantial utility (see utility guidelines, in Federal Register January 5, 2001, Volume 66, Number 5, Pages 1092-1099).

The instant invention is not considered to have a specific and/or substantial utility because the specification fails to establish that "a limulus clotting factor protease-like gene" disclosed in SEQ ID NO 1 encodes a protease as shown by structural and functional properties. The only teaching in the specification regarding the "a limulus clotting factor protease-like gene" is present on page 2 lines 22-26:

> "Recently, an EST was isolated bearing sequence similarity to Limulus clotting factor C precursor (EST accession no. AA833210; G1:2906938)."

On page 8, lines 21-25, it is disclosed that SEQ ID NO 2 is the amino acid sequence for a limulus clotting factor protease like polypeptide, however, the sequence listing does not list any amino acid sequences. It is noted that the

sequence listing has three sequences and all of them are DNA sequences. Therefore, the specification does not provide any evidence that SEQ ID NO 1 encodes a protein or what is the amino acid sequence of the protein. It is emphasized that neither the sequence listing nor the drawings disclose any amino acid sequence. Even if an amino acid sequence was disclosed, the specification does not provide any evidence that the protein encoded by SEQ ID NO 1 is a protease. The specification fails to show a single working example that establishes that the protein encoded by the SEQ ID NO 1 is a protease, by substantial sequence homology and/or functional assay of the protein. No sequence comparisons are taught by specification as filed, nor are any specific similarities to factor C, such as common motifs of conservation, functional motifs etc., functional similarities. Therefore the specification fails to teach that the protein encoded by SEQ ID NO 1 has the biological activity of a factor C related explicitly or implicitly as putatively considered by the specification. In other words, the only immediate apparent utility for a non-human transgenic animal would be for further scientific characterization of the sequence of SEQ ID NO 1 therefore, the claimed invention does not have a substantial utility.

The specification on page 53, lines 1-13 discloses that the homozygous mice displayed a trend towards a decreased response threshold to metrazol and decrease in the response to hot plate test. However, none of these characteristics do not have any relationship to the function of factor C which is a factor in blood clotting pathway. Therefore, utility of the claimed transgenic animals is not specific.

Therefore, the asserted use for the claimed invention is not considered to support by either a specific and/or substantial utility, since no function can be ascribed to the gene whose function has been disrupted in the claimed transgenic non-human animal or mouse and the phenotype of the transgenic animal do not have any correlation to the factor C function.

9. Claims 8-12, 15, and 17-24 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and/ or substantial asserted or a well established utility for the reasons set

forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections - 35 USC § 112

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 8-12, 15, and 17-24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claimed invention is drawn to a transgenic non-human animal comprising a disruption in a limulus clotting factor protease-like gene, a method of producing a transgenic mouse comprising a disruption in a limulus clotting factor protease-like gene, cells of the transgenic mouse/non-human animal and a method of using the transgenic mouse/non-human animal and its cells for identifying agents that modulates the expression of a limulus clotting factor protease-like gene.

While determining whether a specification is enabling, one considers whether the claimed invention provides sufficient guidance to make and use the claimed invention, if not, whether an artisan would have required undue experimentation to make and use the claimed invention and whether working examples have been provided. When determining whether a specification meets the enablement requirements, some of the factors that need to be analyzed are: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill, the level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples, and whether the quantity of any necessary experimentation to make or use the invention based on the content

of the disclosure is "undue" (In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)).Furthermore, USPTO does not have laboratory facilities to test if an invention will function as claimed when working examples are not disclosed in the specification, therefore, enablement issues are raised and discussed based on the state of knowledge pertinent to an art at the time of the invention, therefore skepticism raised in the enablement rejections are those raised in the art by artisans of expertise.

As the current state of the transgenic animal research stands, there are several significant limitations to the application of same methodology of making transgenic animals to different species. Longer gestation times, reduced litter sizes, number of fertilized eggs required for micro injection and relatively low efficiency of gene integration and method of introduction of transgenes are a few examples of such limitations. The variation in expression levels between different cell lines and species may be attributed to host genetic background, the site of chromosomal insertion and absence of specific transcription factors. Cameron (Cameron ER. Molecular Biotechnology 7:253-265, 1997) noted, " Well regulated transgene expression is the key to successful transgenic work, but all too often experiments are blighted by poor levels or the complete absence of expression, as well as less common problems, such as leaky expression in nontargeted tissues. A feature common to many transgenic experiments is the unpredictable transgenic lines produced with the same construct frequently displaying different levels of expression. Further, expression levels do not correlate with the number of transgene copies integrated. Such copy- number-independent expression patterns emphasize the influence of surrounding chromatin on the transgene" (see page 256, section 4 on transgene regulation and expression).

Hammer et al (Hammer RE et al. Cell 63:1099-1112.1990) created both transgenic mice and rats expressing human HLA-b27 gene and beta-2 microglobulin. Although, both the transgenic animals bearing HLA-27 gene expressed the gene, transgenic mice did not show any HLA-2 associated disease whereas the transgenic rats demonstrated most of the HLA-B27 related diseases (see lines 20-28 in col 2 of page 1099). This shows that the integration of a

transgene into alternative species may result in widely different phenotypic responses even in animals of the same species. Additionally, promoters and enhancer elements may not function in all the species because they may require specific cellular factors. The specification does not provide any guidance as to whether a given promoter used for expressing an exogenous gene in one animal would have been functional in other animals and even if the promoter may have been active, whether the level of the transgenic product produced would have been sufficient to produce a certain phenotype. If not, what steps would have been taken to address this issue?

Introduction of foreign DNA into fertilized oocyte , for example by micro injection, may result in random integration of the exogenous DNA into host chromosomal DNA which in turn may have major consequences on the expression of the transgene, therefore the production of transgene in all the non-human mammals species will be highly variable and unpredictable. Even if the transgenic animals are produced, it is highly unpredictable whether transgenic animals from species other than mouse (in the present case) will express the transgene to a level high enough so as to enable the development of the claimed phenotype in the transgenic animals.

The art of culturing and maintaining ES cells in culture is unpredictable. Gardner and Brook (Gardner RL and Brook FA. International J. of Dev. Biol. 41:235-243, 1997) summarized the progress in the field of ES cell biology, "Remarkably little is known about mammalian embryonic stem (ES) cells despite their very widespread use in studies on gene disruption and transgenesis. As yet, it is only in the mouse that lines of ES cells which retain the ability to form gametes following reintroduction into the early conceptus have been obtained. Even in this species, most stains have so far proved refractory to the derivation of cell lines....." Additionally, gene targeting and selection of the ES cells that harbor the integration of a desired construct also has been shown to be unprdictable in animals other than mice. To prevent their differentiation, ES cells are maintained in culture in the presence of mouse derived factors that inhibit differentiation either by coculturing

the cells in the presence of feeder cell lines or by adding agents to the culture as a media supplement. However, it has been suggested that the such differentiation-inhibitory derived from mouse do not adequately prevent differentiation of stem cells in species other than the mouse.

The steps of producing a knockout mouse that include, isolating the gene from a mouse genomic library, destroying the gene by inserting therein a selectable marker gene, introducign vectors incorporated with the destroyed gene into cultured ES cells thereby allowing homologuous recombination to occur, isolating and identying a clone in which homologous recombination has been effected, injecting the clone into a blastocyst that develops into the desired mouse. While the steps to produce knock out mouse have been well developed and used in mice, they have not been fully developed in other animals, particularly the art of gene targeting in ES cells and culture and selection of the ES cells that harbor the desired integration has been shown to be unprdictable in animals other than mice.

It is noted that claim 10 as instantly presented encompasses introducing any cell comprising a targeting cell into a blastocyst for producing a transgenic animal, however, the specification as filed does not provide as to how could any cell be introduced in a blastocyst to produce a transgenic animal. As discussed above making any a transgenic non-human animal except mouse using ES cells was unpredictable, the specification does not teach how to make any transgenic non-human animal from any cell.

The specification on pages 52-54 teaches generation of a homozygous transgenic mouse using a targeting construct described in figure 2 and the transgenic mouse shows decrease in response to latency to hot plate and a decreased response threshold to metrazol, however, there is no evidence as to what is the relationship of the phenotype of the claimed mouse to the protein which was disrupted. While the transgenic mouse displayed changes in pain perception, the presence of these phenotypes in a transgenic mouse may not be predictable of the gene disruption, rather it may be due to genetic background. Lariviere et al (Lariviere et al The Journal of Pharmacology and Experimental Therapeutics 297:467-473, 2001) noted:

"We show that the 129 and C57BL/6 mouse strains, which provide the default genetic background on which null mutants are constructed, display significant and sometimes extreme phenotypic differences in may assays of nociception, hypersensitivity, and analgesia."

It is noted that the mice used in the generation of the instantly claimed mouse were also 129/OlaHsd and C57BL/6. Therefore, the phenotype observed in the mice of the instant invention may be due to genetic variation as discussed by Lariviere et al, and not due to the gene disruption.

Furthermore, Lariviere et al noted that the most common criticism is that compensatory effects of other genes may either mask the detection of the targeted gene's phenotype or alternatively be confused for the phenotype of the null gene (see first paragraph in the left column on page 467). In view of the lack of any information about the function of the disrupted gene in the instant application, it will be unpredictable whether the phenotype observed is due to the gene recited or any other gene.

Therefore, an artisan of skill would not know how to use the claimed transgenic mouse in view of the unpredictability of the phenotype and unpredictability of the relationship of the phenotype to the gene disrupted. Additionally, in view of the unpredictability of the generation of any transagenic animal in general and lack of any relationship of the animal or mouse to the gene disrupted, an artisan of skill would not have known how to use the claimed transgenic animals or mouse. In other words, an artisan of skill would not have been able to practice the claimed methods of identifying agents using the transgenic mouse or transgenic animal.

Therefore, in view of the breadth of the claims and the lack of guidance provided by the specification as well as the unpredictablility of the art, one of ordinary skill in the art at the time of the invention would have required an undue amount of experimentation to make and use any and all embryonic stem cells. It is noted that the unpredictability of a particular area may alone provide reasonbale doubt as to the accuracy of the broad statement made in support of enablement of claims. See Ex parte Singh, 17 USPQ2d 1714 (BPAI 1991).

12. Claims 8-12, 15, and 17-24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claimed invention is drawn to a transgenic non-human animal comprising a disruption in a limulus clotting factor protease-like gene, a method of producing a transgenic mouse comprising a disruption in a limulus clotting factor protease-like gene, cells of the transgenic mouse/non-human animal and a method of using the transgenic mouse/non-human animal and its cells for identifying agents that modulates the expression of a limulus clotting factor protease-like gene.

The specification on pages 52-54 teaches generation of a homozygous transgenic mouse using a targeting construct described in figure 2 and the transgenic mouse shows decrease in response to latency to hot plate and a decreased response threshold to metrazol. As noted in the enablement rejection the mice used in the generation of the instantly claimed mouse were 129/OlaHsd and C57BL/6, therefore the phenotype observed in the mice of the instant invention may be due to genetic variation as discussed by Lariviere et al, and not due to the gene disruption.

In analyzing whether the written description requirement is met, it is first determined whether the whether a representative number of species have been described by their complete structure. Since it is not realistic to expect that the "complete structure" of any transgenic animal, or even a cell, could be described, this requirement is interpreted to be whether phenotypic consequences or other characteristics of the animals resulting from altering the genotype have been described. In the instant case, the claimed invention encompasses knockout non-human transgenic animals including transgenic mouse in which the expression of the recited gene is disrupted. Considering the fact that the phenotype disclosed may not be due to gene disruption and no other phenotype is disclosed, the phenotype(s) of the claimed animals can not be predicted because the art of

making transgenic animals or knockout animals is highly unpredictable. The art teaches that phenotype of a transgenic mouse can not be predicted. Wood (Comparative Medicine 50 (1): 12-15, 2000) noted:

"The phenotype of an animal is determined by a complex interaction of genetics and environment. It is the evaluation of the phenotype that allows us to determine the usefulness of a mutant strain as a model for biomedical research.....A specific phenotype is usually expected from genetically altered mice whether they are transgenic over-expression models or gene knockout models where a particular gene function has been modified or ablated altogether. Thus for any given genetic alteration, we often try to predict what the phenotype will be. Many times we find the predicted phenotypes or more. It is, however, common to hear that surprisingly a given model has "no phenotype"."

This clearly indicates that the phenotype of a transgenic mouse or rat or any animal can not be predicted. Therefore, the specification does not describe the phenotype of a representative number of species of the genus.

Next, it is determined whether a representative number of species have been sufficiently described by other relevant identifying characteristics. In case of a knockout animal, it is not possible to adequately describe the claimed animals because the effects of inactivating a gene cannot be predicted, particularly when a gene product may be interacting with the proteins of a family of proteins. For example, Korach et al (US Patent No. 5,650,550, 7-22-97) produced a knockout mice lacking a functional estrogen receptor. One skilled in the art would not have predicted that such an animal would even be viable (see col 9, lines 22-39), much less have been able to predict the resulting phenotype. In the instant application, what would have been the result of the inactivating mACHR-6 gene cannot be predicted in the transgenic animals encompassed by the invention. With the limited information disclosed in the specification, an artisan would have not been able to predict whether all these animals would have had same or different phenotypes compared to the knockout mice or transgenic mice.

Therefore, the limited disclosure in the specification is not deemed sufficient to reasonably convey to one skilled in the art that Applicants were in possession of

the huge genera recited in the claims at the time the application was filed. Thus it is concluded that the written description requirement is not satisfied for the claimed genera.

13. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

14. Claims 10 and 15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 10 and 15 are indefinite because they are dependent on withdrawn claims and therefore the metes and bounds of the claimed invention are not clear.

15. No claim is allowed.

16. The claimed invention is free of the prior art of record.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ram R. Shukla whose telephone number is (703) 305-1677. The examiner can normally be reached on Monday through Friday from 7:30 am to 4:00 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051. The fax phone number for TC 1600 is (703) 703-872-9306. Any inquiry of a general nature, formal matters or relating to the status of this application or proceeding should be directed to the William Phillips whose telephone number is (703) 305-3413.

Please note that effective January 13, the offices for Examiner Shukla, SPE Reynolds and LIE William Phillips will move to the new USPTO location in

Alexandria, VA and their phone numbers will change. The new phone numbers will be as follows:

Ram Shukla: **(571) 272-0735**

Deborah Reynolds: **(571) 272-0734**

William Phillips: **(571) 272-0548**

Ram R. Shukla, Ph.D.
Primary Examiner
Art Unit 1632

RAM R. SHUKLA, PH.D.
PRIMARY EXAMINER